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Hyperthyroidism as a cause of persistent vomiting

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ABSTRACT

A 32-year-old woman presented with persistent vomiting, epigastric pain and weight loss. A sinus tachycardia was the clue to the diagnosis of hyperthyroidism due to Graves' disease. On treatment with propylthiouracil and a β -blocking agent, her symptoms resolved within one day, even though her free thyroxine level was still high. Hyperthyroidism is an uncommon, but previously reported cause of persistent vomiting.

INTRODUCTION

Thyrotoxicosis is defined as the clinical syndrome that occurs when tissues are exposed to excess amounts of thyroid hormone. Causes of hyperthyroidism are autoimmune thyroid disease, toxic adenoma or toxic multinodular goitre, thyroiditis or overzealous exogenous thyroid hormone intake. In 1835, Graves published his account of 'violent and long-continued palpitations in females in each of which the same peculiarity presented itself, viz., enlargement of the thyroid gland'.¹ Graves' disease is the most common cause of hyperthyroidism; it occurs in up to 2% of women and is ten times less frequent in men. The disorder typically manifests between 20 and 50 years of age, although it also occurs in other age groups.² It is an autoimmune disorder resulting from thyrotropin (TSH)-receptor antibodies, which stimulate thyroid gland growth and thyroid hormone synthesis and release. The classical symptoms of thyrotoxicosis are dyspnoea on exertion, palpitations, tiredness, preference for cold, nervousness, excessive sweating and weight loss.

However, these are nonspecific symptoms. For example, dyspnoea on exertion was found in 81% of patients with hyperthyroidism and in 40% of controls. Palpitations were found in 76% of patients and in 26% of controls in an older British study.³ Specific signs of Graves' disease are ophthalmopathy (clinically obvious in approximately 25% of patients) and pretibial myxoedema, seen in 5% of cases of Graves' disease. Besides the classical, nonspecific symptoms, there are other ways in which thyrotoxicosis can present. In 1976, Rosenthal reported that vomiting can be an important presenting symptom of thyrotoxicosis.⁴ Nevertheless, it is not a well-known phenomenon, as the following case demonstrates.

CASE REPORT

A 32-year-old woman was referred to the outpatient clinic because of persistent vomiting and epigastric pain. Her symptoms had started ten days earlier following a three-day course of prednisone given because of asthmatic symptoms. Metoclopramide, ranitidine, cisapride and domperidone prescribed by her general practitioner had given no relief. She was also taking an oral contraceptive, salbutamol and budesonide by inhaler, and paroxetine, which was started five months earlier because of a mild depression. Recently she had taken two courses of antibiotics for a suspected respiratory tract infection. Physical examination showed a moderately ill woman who weighed 66.5 kg. Her blood pressure was 150/90 mmHg with a pulse rate of 96 beats/min. There was no orthostatic hypotension. There were white patches on the palate,

suspected to be thrush. Examination of the abdomen showed no abnormalities. Laboratory evaluation showed no electrolyte disorders and no signs of dehydration. She refused endoscopy of the upper gastrointestinal tract. Our hypothesis was that she was suffering from *Candida* oesophagitis following antibiotic treatment combined with corticosteroids or from duodenal ulcer or gastritis due to corticosteroid treatment. She was started on famotidine and fluconazol. *Helicobacter* serology turned out to be negative, as did a throat culture on yeast. Three days later she reported dark stools. She was admitted to hospital for observation. She did indeed vomit after eating or drinking. There were no signs of gastrointestinal bleeding, i.e. no melaena or haematemesis. Again she refused endoscopic evaluation. Haemoglobin and calcium levels were normal. The only biochemical abnormality was a mild elevation of the aminotransferases. Pregnancy and hepatitis A and B were ruled out. Ultrasound examination of the abdomen showed no abnormalities. She was discharged still complaining of vomiting and epigastric pain. Six days later she came to the emergency department with the same symptoms. She reported a weight loss of 7 kg. There was no diarrhoea. Her blood pressure and temperature were normal but she had a sinus tachycardia of 134 beats/min. At laboratory evaluation there were once again no signs of dehydration. The aminotransferase levels had normalised. An attempt was made to perform a radiographic examination of her stomach, but this proved to be impossible due to vomiting immediately after swallowing barium contrast. Four days later she was seen at the outpatient clinic. She was carrying a bucket because of the continuous vomiting. She told us that she was eating hardly anything but was able to drink fluids. She denied excessive use of salbutamol. Again, there were no abnormalities on physical examination, except her pulse rate which was 100 beats/min. Because of the tachycardia and the weight loss we thought of hyperthyroidism. The thyroid gland was not enlarged and there was no exophthalmos. The thyroid stimulating hormone (TSH) level turned out to be < 0.01 mE/l, and her free thyroxine level was >75 pmol/l (normal 8-23 pmol/l). Also, the serum aminotransferase levels were increased to five times normal. She was admitted under the diagnosis of thyrotoxicosis and treated with a β -blocking agent (metoprolol 4 dd 100 mg) and propylthiouracil (3 dd 75 mg). Within 24 hours she was free of symptoms after 23 days of continuous vomiting. The free thyroxine level was still 50.7 pmol/l after five days of treatment. The aminotransferase levels normalised within a week. Scintigraphic imaging of the thyroid gland was compatible with the diagnosis of Graves' disease. Six months later she was doing well on thiamazole and levothyroxine without complaining of vomiting or epigastric pain again.

DISCUSSION

The persistent vomiting and epigastric pain of the patient described here were most likely caused by thyrotoxicosis. We cannot rule out other causes with certainty because of the lack of endoscopic and/or radiographic diagnostic imaging. However, she did not respond to treatment with antacids or prokinetic agents while all symptoms resolved completely after treatment of the thyrotoxicosis. Vomiting is not a well-known symptom of hyperthyroidism. In *Harrison's Textbook of Internal Medicine* vomiting is not mentioned as a symptom of thyrotoxicosis (table 1).²

Table 1
Signs and symptoms of thyrotoxicosis (in descending order of frequency)²

Symptoms
Hyperactivity, irritability, dysphoria
Heat intolerance and sweating
Palpitations
Fatigue and weakness
Weight loss with increased appetite
Diarrhoea
Polyuria
Oligomenorrhoea, loss of libido
Signs*
Tachycardia; atrial fibrillation in the elderly
Tremor
Goitre
Warm, moist skin
Muscle weakness, proximal myopathy
Lid retraction or lag
Gynaecomastia

*Excludes the signs of ophthalmopathy and dermopathy specific for Graves' disease.

Nevertheless, Rosenthal *et al.* reported on seven cases in 1976.⁴ After that, several case reports have been published describing persistent vomiting due to hyperthyroidism. In a number of the reported cases Graves' disease was the cause of excess thyroid hormone production; however in some cases the cause of the hyperthyroidism was not specified (table 2).⁵⁻¹² Werner and Ingbar's *The Thyroid* mentions thyrotoxic vomiting when describing gastrointestinal symptoms in hyperthyroidism. Furthermore, it is stated that clinical and experimental data on the effect of thyrotoxicosis on gut motility provide some evidence that thyroid excess affects the orderly propulsion

Table 2
Case reports of thyrotoxic vomiting

AUTHOR	SEX	AGE	MAIN SYMPTOMS	CAUSE OF HYPERTHYROIDISM
Rosenthal <i>et al.</i> ⁴	F	41	Vomiting, abdominal pain	Graves' disease
	F	35	Vomiting	Graves' disease
	F	49	Vomiting	Graves' disease
	F	66	Vomiting	Nodular thyroid disease
	F	57	Vomiting	Graves' disease
	F	66	Vomiting	Graves' disease
	M	54	Vomiting	Not specified
Dreyfuss ⁵	F	53	Epigastric pain, vomiting	Graves' disease
Desai <i>et al.</i> ⁶	M	54	Vomiting	Graves' disease
Muller <i>et al.</i> ⁸	M	12	Vomiting	Not specified
Canslar <i>et al.</i> ¹⁰	F	35	Vomiting, abdominal distention	Not specified
Chen <i>et al.</i> ¹¹	M	40	Vomiting	Graves' disease
Parkin <i>et al.</i> ¹²	M	43	Vomiting, weight loss	Graves' disease
Hoogendoorn <i>et al.</i>	F	32	Vomiting	Graves' disease

of ingested materials through the gastrointestinal tract.¹³ Harper carried out a retrospective chart review of 25 patients hospitalised for thyrotoxicosis and found that 44% reported vomiting and 20% complained of abdominal pain.¹⁴ Of notion is that one or more of these abdominal symptoms were included as a chief complaint in 36% of cases reviewed.

The mechanism that causes vomiting in thyrotoxicosis is not clear. Suggestions are direct action of excess thyroid hormone on gastrointestinal motility or thyroid hormone stimulation of a chemoreceptor trigger zone in the central nervous system.¹³ Of interest is the relationship with hyperemesis gravidarum, a syndrome of nausea and vomiting associated with weight loss of 5% or more during early pregnancy that occurs in 0.1 to 0.2% of pregnancies. Elevated serum FT₄ and T₃ concentrations are a common finding in women with hyperemesis gravidarum. The placenta secretes hCG, a glycoprotein hormone sharing a common alpha subunit with TSH but having a unique beta subunit, which confers specificity. It is known that hCG has thyroid-stimulating activity.¹⁵ Women who develop hyperemesis gravidarum have higher serum hCG and oestradiol concentrations than do normal pregnant women. The hCG of women with hyperemesis seems to have even more thyroid-stimulating activity because more of it is desialyated.¹⁶ Therefore, serum TSH concentrations are more often low in women with hyperemesis than in normal pregnant women¹⁷. A few of these women have high serum free T₄ concentrations. The elevated FT₄ could contribute to the vomiting of hyperemesis gravidarum in those women.

Another possible mechanism behind thyrotoxic vomiting, besides direct action of thyroid hormone on gastric motility

or on the chemoreceptor trigger zone, could be the increase in β -adrenergic activity in hyperthyroidism due to an increased number of β -adrenergic receptors.¹⁸ The increase in β -adrenergic activity is responsible for many of the other symptoms associated with hyperthyroidism. It also explains the ability of β -blockers to cause a rapid improvement in many of the symptoms, including palpitations, tachycardia, tremulousness, anxiety, and heat intolerance. In support of the theory that vomiting is caused by β -adrenergic stimulation is the observation Dreyfuss made in a 53-year-old woman who suffered from epigastric pain and vomiting due to hyperthyroidism.⁵ He noted that after 36 hours of treatment with propranolol and propylthiouracil, the symptoms had resolved completely, while the thyroxine level was still high. This was also seen in our patient.

Rosenthal *et al.* reported on seven patients with thyrotoxic vomiting.⁴ Four of the seven patients showed elevated liver enzymes values. This was also the case in the patient described here. It is not clear by which mechanism this is caused. Possible thyroid-liver interactions include liver damage secondary to the systemic effects of thyroid excess or direct toxic effects of thyroid hormone on the liver.¹³ The abnormal values were reversed to normal within a week of starting treatment.

CONCLUSION

Persistent vomiting and epigastric pain can be symptoms of thyrotoxicosis. The symptoms resolve quickly and completely with treatment with β -blocking agents and antithyroid drugs.

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